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US 4925655 A
Biosis Abstract No.97400125 & Oral Microbiol and
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(54) Compositions containing tea tree oil

(57) Compositions containing oil from plants of the genus MELALEUCA (tea tree) have activity against oral infections e.g ulcers, gingivitis and periodontal disease. The preferred compositions comprise the oil, water and a surfactant.

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TREATMENT OF ORAL INFECTIONS

The present invention relates to substances and compositions for use in the treatment of oral infections, especially gingival infections, periodontal infections and ulcers, particularly types of gingivitis including acute necrotising ulcerative gingivitis, periodontitis and aphthous ulcers.

Tea tree oil, also known as Melaleuca oil, is obtained from the leaves of the Australian tea tree, Melaleuca alternifolia. The oil is sometimes referred to as Australian tea tree oil, oleum Melaleucae or ti-tree oil. The entry for Melaleuca oil on page 1385 of Martindale - The Extra Pharmacopoeia (13th edition) ed. Reynolds J.E.F., The Pharmaceutical Press, London (1993) states that the oil is reported to have bactericidal and fungicidal properties. The oil can be used topically to treat a variety of skin disorders.

Tea tree oil is also known to be useful in surgery, medicine and dentistry and the oil has been included in some medicated soaps and dentrifices.

Tea tree oil has been used with beneficial effect in the treatment of a variety of human ailments and conditions. For example, dandruff, blisters, corns, bruises, burns, insect bites, ringworm, minor finger infections, pierced ear infections, fungal infections such as athletes foot, ingrowing hair, ingrowing toenails, warts, dermatitis, eczema, shingles, psoriasis, heat rash, itching, spots, acne, cuts, grazes, chicken pox, headache, blocked sinuses, the common cold, influenza, sprains and strains, haemorrhoids and teething in infants.

There are a number of commercially available preparations which include tea tree oil. These preparations are Secaderm produced by Fisons for the treatment of chilblains, Soothene produced by Lane for the treatment of minor skin disorders and Tubérol syrup produced by Bouteille (France) for the treatment of coughs.

The oil has found use as an insect repellent and in saunas where it is dispersed into the air. The oil is also known to have veterinary applications in the treatment of hot spots, flea infestation, infected flea bites, ticks, lice, hoof thrush, skin irritations and roundworm.

Acute necrotising ulcerative gingivitis, also called Vincent's infection or trench mouth, is an oral infection which is known to be caused by fusiform bacteria and spirochaetes. Metronidazole is known to be useful in treating acute necrotising ulcerative gingivitis. Metronidazole is given to the patient orally in 200mg doses three times daily for three days. Similar doses are used in acute dental infections. Metronidazole has a number of adverse effects on patients and these are generally dose-related. The most common are gastro-intestinal disturbances, especially nausea. The nausea is sometimes accompanied by headache, anorexia and vomiting. An unpleasant metallic taste may be experienced. Where high doses or prolonged treatments are undertaken, peripheral neuropathy, usually presenting itself as a numbness or tingling of the extremities occurs. Also, epileptic-like seizures and serious adverse effects on the nervous system have been encountered.

Periodontal diseases are infections of the periodontium which may progress. Tetracycline can be used systemically in the treatment of periodontal disease but on termination of the treatment the benefits are limited. The

infection can reoccur and the antibiotic does not take the place of active periodontal treatment e.g. curettage and surgery. The topical application of tetracycline to an infected region is also known to be effective. In the
5 topical treatment, absorbent fibrous material loaded with tetracycline is tied around the teeth of a patient which are associated with the infection. However, this method of treatment suffers from the drawback that it is time consuming and awkward for the patient. Systemic
10 tetracycline administration can also give rise to side effects such as nausea, vomiting and diarrhoea. The patient can become resistant to this antibiotic with continual topical treatment.

15 In less severe cases of gingivitis, a chlorhexidine mouthwash or dental gel is known to be a useful treatment. Chlorhexidine at 0.1% (w/v) to 0.2% (w/v) used two or three times daily is known to reduce gingivitis and periodontal disease. Chlorhexidine suffers from the disadvantage that
20 its use is limited by its unpleasant taste and staining properties.

The inventor has found that tea tree oil can be used to treat oral infections effectively and apart from an
25 unpleasant taste, the oil has no apparent side effects.

Accordingly, the present invention provides the use of oil obtained from plants of the genus Melaleuca in the manufacture of a medicament for the treatment of oral
30 infections. The term oral infection also includes fungal infections e.g. Candida infections. The medicament is preferably of use in the treatment of ulcers, gingival infections including acute necrotising ulcerative gingivitis, and periodontal infections. In particular, the
35 medicament may be used in the treatment of aphthous ulcers, gingivitis and periodontitis.

The plants are preferably those which are commonly known as tea trees. The plants may also be known by the name Australian Melaleuca.

5 The plants may be one or more of Melaleuca alternifolia, M. uncinata, M. cajuputi, M. viridiflora, M. quinquenervia and M. bracteata.

10 The oil may be obtained from a single plant or from a number of individual plants. When the oil is obtained from a number of individual plants, the plants are preferably of the same species. However, the plants may comprise more than one species of Melaleuca.

15 The oil is preferably obtained from the leaves of the plants but the oil may also be obtained from any other oil bearing parts such as whole shoots and stems. Preferably, the oil is distilled from the oil bearing parts. Prior to distillation the oil bearing parts may be pressed or
20 crushed in order to release the oil from the plant. Alternatively, the plant parts may be comminuted and extracted with water or an organic solvent before distillation.

25 Melaleuca oil which is a preferred oil is known to comprise about 50 to 60% by weight of terpenes, up to 10% by weight cineole and some terpineol. Other oils which may be used in the present invention may comprise terpenes, cineole and terpineol in different proportions to that found in Melaleuca oil.

30 The medicament is preferably in the form of a liquid comprising tea tree oil, water and a pharmaceutically acceptable surfactant. The surfactant is preferably a non-ionic surfactant although a suitable ionic surfactant may
35 be used. More than one surfactant may be present and both

ionic and non-ionic surfactants may be present together. A preferred non-ionic surfactant is nonylphenol.

5 The medicament may further comprise an alcohol and a preferred alcohol is ethanol. Other pharmaceutically acceptable alcohols may be used instead of ethanol or in combination with ethanol. The medicament may also further comprise an ethoxylate.

10 The present invention also provides a method of treating oral infections comprising exposing diseased areas of the patient to oil obtained from plants of the genus Melaleuca. The oral infections may be ulcers, gingival infections and periodontal infections, particularly
15 aphthous ulcers, gingivitis and periodontitis. The oral infection may be fungal e.g. Candida. The oil is preferably in the form of a medicament as hereinbefore described.

20 Preferably, the medicament may be applied to the periodontal tissues and gums of the patient in the form of a mouthwash. When the medicament is to be used as a mouthwash it is preferably diluted to a suitable working strength with water. Alternatively, the medicament may be
25 applied directly to the infected areas of the patient using an absorbent material such as cotton wool, an interdental appliance or various types of dental floss.

30 The invention will now be described with reference to the following example.

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EXAMPLE 1 The treatment of acute destructive
periodontal disease (Periodontitis Complex Type IV)
with Australian Melaleuca oil.

5 An elderly male patient suffering from severe
periodontal disease (Periodontitis Complex Type IV) was
treated with tea tree oil. The oil used was the
commercially available Thursday Plantation tea tree oil
antiseptic, mild strength formulation, comprising 15% (v/v)
10 Australian Melaleuca oil (tea tree oil). (Thursday
Plantation P/L., Pacific Highway, Ballina 2478, Australia.)
The tea tree oil solution also comprises water,
nonylphenol, an ethoxylate and ethanol.

15 A previous attempt at treating the patient's condition
with a standard treatment of oral hygiene and visits to a
dental hygienist for a period of 28 days was unsuccessful.
At the start of the tea tree oil treatment the patient had
deep pockets of infection around his teeth and his gums
20 were swollen, painful and bleeding. Several teeth were
loose. Surgical intervention was proposed in order to
remove the swollen and infected periodontal tissues
throughout the periodontium. At this time root and
epithelial curettage were also planned to further remove
25 the infected tissues and the infected root surface.

As an alternative to the surgical intervention, a
mouthwash of tea tree oil solution was made up by diluting
1 part of solution from the bottle with approximately 1
30 part tap water. The patient took a mouthful of mouthwash
and agitated this in his mouth for approximately 2 minutes
after which time the mouthwash was released by the patient
from his mouth. The mouthwash treatment was repeated twice
daily for 28 days accompanied by good oral hygiene
35 maintenance by the patient. At the end of the treatment
the patient's teeth and gums appeared to be in a healthy

condition. The periodontal infection was resolved. The gingivae had a normal appearance and the periodontal pockets had reduced 3-5mm in areas which were previously severely infected.

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EXAMPLE 2

10 A female patient aged 63, a periodontist, noted a periodontal infection between the lower right lateral and cuspid teeth. The gum tissue was swollen, bleeding and painful.

15 The infected area was treated repeatedly by the direct application of tea tree oil on an interdental appliance over a period of two days. The lesion totally resolved after two days treatment and did not recur. The periodontist considered that this confirmed the result of Example 1.

CLAIMS

1. The use of oil obtained from plants of the genus Melaleuca in the manufacture of a medicament for the treatment of oral infections.
2. A use as claimed in Claim 1, wherein the medicament is for the treatment of ulcers, gingival infections and periodontal infections.
3. A use as claimed in Claim 2, wherein the medicament is for the treatment of aphthous ulcers, gingivitis and periodontitis.
4. A use as claimed in any one of Claims 1 to 3, wherein the plants are tea trees.
5. A use as claimed in Claim 4, wherein the plants are Australian Melaleucas.
6. A use as claimed in any one of Claims 1 to 3, wherein the plants are one or more of Melaleuca alternifolia, M. uncinata, M. cajuputi, M. viridiflora, M. quinquenervia and M. bracteata.
7. A use as claimed in any one of Claims 1 to 6, wherein the oil is obtained from the leaves of the plants.
8. A use as claimed in Claim 7, wherein the oil is distilled from the leaves.
9. A use as claimed in any preceding claim, wherein the medicament is a solution comprising the oil, water and a pharmaceutically acceptable surfactant.
10. A use as claimed in Claim 9, wherein the medicament

further comprises an alcohol.

11. A use as claimed in Claim 9 or Claim 10, wherein the alcohol is ethanol.

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12. A use as claimed in any one of Claims 9 to 11, wherein the medicament further comprises an ethoxylate.

13. A method of treating oral infection comprising exposing diseased areas of the patient to oil obtained from plants of the genus Melaleuca.

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14. A method as claimed in Claim 13, wherein the oral infection is an ulcer or ulcers, gingival infection or periodontal infection.

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15. A method as claimed in Claim 14, wherein the oral infection is aphthous ulcers, gingivitis or periodontitis.

16. A method as claimed in any one of Claims 13 to 15, wherein the plants are tea trees.

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17. A method as claimed in Claim 16, wherein the plants are Australian Melaleucas.

25

18. A method as claimed in any one of Claims 13 to 15, wherein the plants are one or more of Melaleuca alternifolia, M. uncinata, M. cajuputi, M. viridiflora, M. quinquenervia and M. bracteata.

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19. A method as claimed in any one of Claims 13 to 18, wherein the oil is obtained from the leaves of the plants.

20. A method as claimed in Claim 19, wherein the oil is distilled from the leaves.

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21. A method as claimed in Claim 20, wherein the oil is part of a solution comprising the oil, water and a pharmaceutically acceptable surfactant.

5 22. A method as claimed in Claim 21, wherein the solution further comprises an alcohol.

23. A method as claimed in Claim 22, wherein the alcohol is ethanol.

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24. A method as claimed in any one of Claims 21 to 23, wherein the solution further comprises an ethoxylate.

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Patents Act 1977
Examiner's report to the Comptroller under Section 17
(The Search report)

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Relevant Technical Fields

- (i) UK CI (Ed.N) A5B (BE)
(ii) Int CI (Ed.6) A61K 35/78

Search Examiner
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Databases (see below)

(i) UK Patent Office collections of GB, EP, WO and US patent specifications.

(ii) ONLINE: WPI, CLAIMS, CAS ONLINE, JAPIO, BIOSIS, EMBASE, MEDLINE

Documents considered relevant following a search in respect of Claims :-
1-12

Categories of documents

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| <p>X: Document indicating lack of novelty or of inventive step.</p> <p>Y: Document indicating lack of inventive step if combined with one or more other documents of the same category.</p> <p>A: Document indicating technological background and/or state of the art.</p> | <p>P: Document published on or after the declared priority date but before the filing date of the present application.</p> <p>E: Patent document published on or after, but with priority date earlier than, the filing date of the present application.</p> <p>&: Member of the same patent family; corresponding document.</p> |
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Category	Identity of document and relevant passages	Relevant to claim(s)
X	US 4925655 (ROBELL) see abstract column 3 lines 4-5 column 1 lines 37-39	1, 2, 4
A	Biosis Abstract No 97400125 & Oral Microbiol and Immunol 9(4), 1994, pages 202-208	1

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